

REMARKSRejection of Claims 4-8, 10, 12-22, 25, 26, newly amended Claims 1-3, 9, 11, 23, 24 and newly added Claims 27-52

Claims 4-8, 10, 12-22, 25, 26, newly amended Claims 1-3, 9, 11, 23, 24 and newly added Claims 27-52 are rejected under 35 U.S.C. §112, first paragraph "for lack of adequate written description of the invention" (Office Action, page 2). The Examiner states that the rejection to a genus of antimicrobial peptides is maintained "because the specification fails to provide adequate written description as to the characteristic features how a structural changes [sic] may influence the biological activity of AMP derivatives" (Office Action, page 3). Citing Rivet *et al.*, Perez-Paya *et al.* (1994) and Perez-Paya *et al.* (1995), the Examiner states that "the antimicrobial activity of melittin analogues will vary significantly depending on the position and components of amino acid residues" (Office Action, pages 3-4). Referring to the variation in the experimental results in Applicants' disclosure, the Examiner states that the "specification fails to teach why these variation occurred and what kind of partial or combination of these derivatives will have antimicrobial activity" (Office Action, page 4). The Examiner further states that Applicants' "recited 'AMP and their derivatives' in the claim surely encompass a large number of peptides, but their structural-functional relationship is not disclosed in the specification" (Office Action, page 4). The Examiner concludes that the "information provided by the specification is not sufficient to enable one skill in the art recognize that the applicants had possession of the claimed invention as a whole at the time the application was filed and the priority is claimed" (Office Action, page 5).

Applicants respectfully disagree. The court has clearly stated that a specification need not describe -- and best omits -- that which is well-known in the art (*In re Buchner* 18 U.S.P.Q.2d 1331, 1332 (Fed. Cir. 1991)). Nevertheless, in the specification as filed, Applicants have provided adequate written description of characteristic features and structural changes that influence the biological activity of AMP derivatives. For example, in the specification as filed, Applicants teach that:

SB-37 (a close cecropin B analogue) and Shiva-1 (a cecropin B analogue that shares 40% sequence homology and maintains the same charge distribution and hydrophobicity as the peptide) have been shown to lyse several mammalian leukemia and lymphoma cell lines *in vitro* (specification, page 4, lines 7-14).

In addition, Applicants teach that:

melittin analogues wherein at least the last six terminal (C-terminal) amino acids is altered and replaced by six glycine residues appear to have a therapeutic benefit similar to melittin, these amino acid analogues have a structure of Gly-Ile-Gly-Ala-Val-Leu-Lys-Val-Leu-Thr-Thr-Gly-Leu-Pro-Ala-Leu-Ile-Ser-Trp-Ile-Gly-Gly-Gly-Gly-Gly (SEQ ID NO:2) (specification, page 9, lines 24-30).

Applicants also teach "Amfi 1 or 2 and peptides of GP 41 that are melittin-like" (specification, page 10, lines 5-6) and that "the structural analogues of melittin include an amphophilic helix with or without signal peptide and activation domains" (specification, page 10, lines 18-20). Therefore, in the specification as filed, Applicants provide examples of how antimicrobial peptides can be modified and so that biological activity is retained.

Furthermore, at the time of Applicants' invention methods of obtaining a *biologically active derivative which is a part, analogue or homologue of an antimicrobial peptide* are well known to those of skill in the art. At the time of Applicants' invention, there was a substantial amount of readily available information in this field of art that provides a solid basis for making reasonably accurate predictions about peptides which are biologically active parts (portions), analogues or homologues of an antimicrobial peptide. In addition, methods for assessing whether a particular part (portion), analogue or homologue of an antimicrobial peptide is biologically active were also known at the time of Applicants' invention (*e.g.*, see Perez-Paya *et al.*, 1995, under the heading "Hemolytic and Antimicrobial Assays").

For example, one of ordinary skill in the art can reasonably predict that deleting a single amino acid from one of the ends of an antimicrobial peptide (*i.e.*, the first or last amino acid) would likely produce a portion of an antimicrobial peptide that retains biological activity. In addition, exchanging an amino acid of an antimicrobial peptide with a similar amino acid (*e.g.*, an amino acid with the same charge) particularly outside the catalytic center of a microbial peptide is well tolerated. Such modifications, which do not affect the function of antimicrobial peptides were known at the time of Applicants' invention. As pointed out above, analogues of

cecropin B are readily disclosed which have as little as 40% sequence homology to the original cecropin B and still remain functional (specification, page 4, lines 7-14). At the time of the present invention, it was known that cecropin analogues having the same charge distribution and hydrophobicity as an antimicrobial peptide retains biological activity. As also pointed out above, Applicants teach that melittin analogues are functional particularly when the last six C-terminal amino acid residues are replaced by glycine (page 9, lines 24-30) and/or comprise an amphiphilic helix with or without signal peptide and activation domains (page 10, lines 18-20).

The art cited by the Examiner show that at the time of the present invention, the skilled practitioner could 1) *predict* which modifications would or would not produce biologically active analogues of antimicrobial peptides, 2) make biologically active analogues of antimicrobial peptides and 3) assess whether such analogues of antimicrobial peptides were biologically active. For example, Perez-Paya *et al.* (Biochem. J. 1994) studied the hemolytic activity of different melittin analogues and showed the structure-function relationship of melittin and a number of melittin analogues. Perez-Paya *et al.* (Biochem. J. 1994) teach that:

[v]ariation in amphipathicity can be correlated with changes in calculated hydrophobic moment... ***The hydrophobic moment of a variety of peptides have been reported to correlate well with their biological activities...*** In the present study, the decreases found in the hydrophobic moments relative to melittin for the two omission analogues (omW19 and omW120) correlated with their decrease in hemolytic activity... Furthermore, the hemolytic activities of these two analogues correlated well with their lack of folding in the presence of increasing salt concentration or of micelles (Perez-Paya *et al.*, Biochem. J., 1994; page 589, column 2- page 590, column 1, emphasis added).

Perez-Paya *et al.* (Biochem. J. 1994) teach, for example, that substitutions on the hydrophilic face of an assumed α -helix with hydrophobic residues (subP14W) are generally well tolerated whereas substitutions with less hydrophobic residues on the hydrophobic face often result in the inactivation of the peptide (Perez-Paya *et al.*, Biochem. J. 1994; page 590, second column, 2nd paragraph). Indeed, Perez-Paya *et al.* (Biochem. J., 1994) teach melittin analogues, such as the subK7D analogue of melittin which “showed the most melittin-like behaviour” (Perez-Paya *et al.*, Peptide Res. 1994; page 588, column 2) and the subP14W analogue which was more active than the naturally occurring melittin (*i.e.*, subP14W). Clearly, at the time of Applicants’

invention, the skilled practitioner could predict and make biologically active analogues of melittin, and could apply such knowledge to other known antimicrobial peptides.

Perez-Paya *et al.* (Peptide Res. 1994) discuss approaches to the design of new synthetic enzyme-like peptides using binding-step based mimics. As a model, Perez-Paya (Peptide Res. 1994) selected melittin to “evaluate the importance” of its “binding affinity to phospholipid membranes” (Perez-Paya *et al.* (Peptide Res. 1994, page 287, column 2) and purposely selected the subK7I melittin analogue, which was ***predicted and shown*** by Perez-Paya *et al.* (Biochem. J. 1994, page 589, column 2) to have decreased biological activity based on its decreased hydrophobic moment and low binding affinity to phospholipid membranes, for comparison.

Perez-Paya *et al.* (1995) teach that substitutions preventing the inducible amphipathic folding ability of melittin, result in the loss of hemolytic and antimicrobial activity (Abstract). In particular, Perez-Paya *et al.* examined “the effects of altering the degree of amphipathicity on the folding process, as well as the membrane binding ability of peptides” (Perez-Paya *et al.*, Discussion, 1st paragraph). Perez-Paya *et al.* state that:

[s]ince position 7 of melittin’s sequence is fully exposed to the solvent in melittin tetramer and, in turn, is distant from the hydrophobic core (9, 10), ***the use of single substitution analogues at position 7 was expected to provide insight*** into the early steps of the folding and self association process (Perez-Paya *et al.*, Discussion, 1st paragraph, emphasis added).

Rivett *et al.* provides further evidence that those of skill in the art knew what modifications could be made to an antimicrobial peptide of known structure to retain its biological activity. For example, Rivett *et al.* teach that:

[c]ytolytic activity of melittin analogues comprising the full 26 residues could be obtained with ***wide sequence permutations providing that a general amphipathic helical structure was preserved*** (Rivett *et al.*, abstract).

On page 529, left column, last paragraph, Rivett *et al.* summarize that “a lytic peptide with activity approaching that of melittin can be produced from an approximately 21-residue amphipathic peptide provided that the N-terminal amino-group remains free and the peptide includes a lysine or arginine residue at position 7, a proline at position 14 and probably an aromatic residue at position 19”. Rivett *et al.* show that at the time of Applicants’ invention,

those of skill in the art had available concrete instructions about how a melittin analogue can be modified in order to retain biological activity.

Using Applicants' specification and the substantial amount of knowledge readily available in this field of art at the time of Applicants' invention, a person of skill in the art could make a biologically active derivative which is a part, analogue or homologue of an antimicrobial peptide using routine skills. Analogues of the antimicrobial peptides are described in the state of the art documents and other analogues can be identified without undue experimental burden since detailed disclosure about the structural-functional relations of amino acid residues of several antimicrobial peptides are available.

Clearly, Applicants' specification meets the written description requirement of 35 U.S.C. §112, first paragraph.

Rejection of Claims 1-52 under 35 U.S.C. §112, first paragraph

Claims 1-52 are rejected under 35 U.S.C. §112, first paragraph "for lack of enablement to its full scope" (Office Action, page 5). The Examiner states that "the specification fails to provide sufficient guidance regarding how to make a partial or combination, an analogue or homologue of AMPs so that these derivatives will be indeed capable of killing microorganisms" (Office Action, page 5). The Examiner states that the recited claims "encompass a large number of peptides, but their structural functional relationship is not disclosed in the specification" and that "without detailed disclosure about the structural-functional relations, the results of making these derivatives will be highly unpredictable" (Office Action, page 5).

Applicants respectfully disagree. The court has clearly stated that:

Enablement is not precluded by the necessity for experimentation such as routine screening... However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue' not 'experimentation'... The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness having due regard for nature of the invention and the state of the art... The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed (In re Wands, 1400 U.S.P.Q.2d 1400, 1404 (CAFC 1988)).

As pointed out above, using Applicants' specification and the substantial amount of knowledge readily available in this field of art at the time of Applicants' invention, a person of skill in the art could make a biologically active derivative which is a part, analogue or homologue of an antimicrobial peptide using routine skills. Analogues of the antimicrobial peptides are described in the state of the art documents and other analogues can be identified without undue experimental burden since detailed disclosure about the structural-functional relations of amino acid residues of several antimicrobial peptides are available.

As also pointed out above, at the time of Applicants' invention, there was a substantial amount of readily available information in this field of art that provides a solid basis for making reasonably accurate predictions about peptides which are biologically active parts (portions), analogues or homologues of an antimicrobial peptide. The art cited by the Examiner in support of the 35 U.S.C. 112, first paragraph written description rejection show that at the time of the present invention, the skilled practitioner could 1) predict which modifications would or would not produce biologically active analogues of antimicrobial peptides, 2) make biologically active analogues of antimicrobial peptides and 3) assess whether such analogues of antimicrobial peptides were biologically active (*e.g.*, see Perez-Paya *et al.*, 1995, under the heading "Hemolytic and Antimicrobial Assays").

For example, one of ordinary skill in the art can reasonably predict that deleting a single amino acid from one of the ends of an antimicrobial peptide (*i.e.*, the first or last amino acid) would likely produce a portion of an antimicrobial peptide that retains biological activity. In addition, exchanging an amino acid of an antimicrobial peptide with a similar amino acid (*e.g.*, an amino acid with the same charge) particularly outside the catalytic center of a microbial peptide is well tolerated. Such modifications, which do not affect the function of antimicrobial peptides were known at the time of Applicants' invention. As pointed out above, analogues of cecropin B are readily disclosed which have as little as 40% sequence homology to the original cecropin B and still remain functional (specification, page 4, lines 7-14). At the time of the present invention, it was known that cecropin analogues having the same charge distribution and hydrophobicity as an antimicrobial peptide retains biological activity. As also pointed out above, Applicants teach that melittin analogues are functional particularly when the last six C-terminal amino acid residues are replaced by glycine (page 9, lines 24-30) and/or comprise an amphiphilic

helix with or without signal peptide and activation domains (page 10, lines 18-20). Thus, Applicants' disclosure which references documents that describe the claimed analogues enables the skilled practitioner to produce biologically active analogues of antimicrobial peptides such as cecropin.

Clearly, in the specification as filed Applicants have provided a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Moreover, the experimentation needed to produce the claimed biologically active derivative which is a part, analogue or homologue of an antimicrobial peptide and to assess its biological activity is merely routine to a person of skill in the art.

The Examiner further states that "not all tumors have a viral related pathogenesis and the art known knowledge is that AMPs are powerful in killing bacterial organism and fungi, only some of them such as defensin shown [sic] some antiviral activity (*Bowman*, pg 79, 2nd paragraph) at the time the application claimed priority" (Office Action, page 5).

Applicants have provided working examples demonstrating that administration of a retroviral vector comprising a sequence which codes for antimicrobial peptides (*e.g.*, melittin, cecropin) produces anti-tumor effects *in vivo* and anti-retroviral effects *in vitro*. Applicants' data, which also shows that the claimed construct was successfully delivered and that the antimicrobial peptide was expressed *in vivo* in an acceptable animal model, is recognized in the art as reasonably correlating to the claimed invention. The court has stated that "it is incumbent upon the Patent Office, whenever a [112 enablement] rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement" (*In re Marzocchi & Horton* 169 U.S.P.Q. 367, 370 (CCPA 1971)). Where is the evidence that is inconsistent with Applicants' claimed invention that is directed to treatment of tumors that do not necessarily exhibit a viral related pathogenesis using antimicrobial peptides; or evidence that is inconsistent with Applicants' claimed invention that is directed to treatment of viruses using antimicrobial peptides other than defensin?

The Examiner states that the recitation of “cell cycle regulatory peptides, tumor suppressor peptides, antiproliferation peptides and cytokines” in Claims 8 and 34 “is not supported by the specification” (Office Action, page 6).

Applicants respectfully disagree. DNA which encodes cell cycle regulatory peptides, tumor suppressor peptides, antiproliferation peptides or cytokines (specification, page 14, lines 2-5 of the specification as filed) are well known in the art. Furthermore, it is well within the skill in the art to obtain such DNA and introduce it into a polylinker of a retroviral vector.

Applicants have provided an enabling disclosure for the full scope of the claimed invention.

Rejection of Claims 1-52 under 35 U.S.C. §112, first paragraph

Claims 1-52 are rejected under 35 U.S.C. §112, first paragraph “for lack of enablement of the claimed invention” (Office Action, page 6). The Examiner states that “the specification fails to provide any guidance as to whether the *in vivo* use of AMPs, their analogues, homologues and combinations thereof, will provide such antitumor and antiviral effect with a reasonable success and an acceptable level of side effects” (Office Action, page 6). The Examiner states that:

[t]he *in vivo* working example in the specification is a pure experimental approach investigating the expression of AMPs and their derivatives to the growth of the transduced tumor cells. The model itself does not provide a method of treating a disease in a mammal with a naturally occurred “genetic defect, cancer and viral infections” (Office Action, page 7).

The Examiner further states that the “incidence of tumor after these cell-line injections shows large variations in figures 9 and 10” (Office Action, page 7). It is the Examiner’s opinion that “the means and ways to treat a naturally occurred genetic defect, a tumor or a viral infection, which is essential to the claimed invention, are not disclosed in the specification” (Office Action, page 7). In addition, the Examiner states that “[a]ll AMPs and their derivatives, which have an antimicrobial and antitumor activity, will also have a cytotoxic effect to the host” and the effect to normal cells of host “has not been disclosed by the applicants, therefore, the method is not enabled to use *in vivo* therapeutically” (Office Action, page 8).

Applicants respectfully disagree. The Examiner has not met her burden of providing acceptable evidence to show that Applicants have not provided an enabling disclosure for the full scope of the claimed invention. Applicants have provided working examples demonstrating that administration of a retroviral vector comprising a sequence which codes for antimicrobial peptides (*e.g.*, melittin or cecropin) produces anti-tumor effects *in vivo* and anti-retroviral effects *in vitro*. In the previously filed Amendment A mailed to the Patent Office on September 20, 1999, Applicants pointed out that their data is recognized in the art as reasonably correlating to the claimed invention (see, for example, Bowman, page 83) and cited the *Brana* case in support thereof.

The court has recognized that:

the context of pharmaceutical inventions, necessarily includes the expectation of further research and development (*In re Brana*, 34 U.S.P.Q.2d 1436, 1442 (CAFC 1995).

The court also recognized that to require testing more suited to review by the FDA would involve costs that

would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer” (*Id.* At 1443).

Applicants’ data show that the claimed construct was successfully delivered and that the antimicrobial peptide was expressed *in vitro* and *in vivo* in an acceptable animal model, *and* that the antimicrobial produced antitumor and antiretroviral effects. Where is the evidence that one of skill in the art would not find that Applicants’ *in vivo* model correlates to “a method of treating a disease in a mammal with a *naturally occurred* genetic defect, cancer and viral infections”?

Furthermore, some variation is expected when an animal model is treated with a retroviral vector and does not at all contravene a method of treatment claim. Retroviral vectors integrate randomly into a host cell genome, *i.e.*, in this case in the EJ cell genome. Since the activity of a gene transferred by a retroviral vector, *i.e.*, in this case the gene encoding the antimicrobial peptide, largely depends on the position, where the retroviral vector is inserted in the host cell genome, it was expected that different EJ cell clones, in which the retroviral vector was integrated in different positions, would express different amounts of the antimicrobial peptides.

Consequently, it was expected that some EJ cell clones would strongly express the antimicrobial peptide and hence would inhibit tumor growth, whereas other EJ cell clones would express small amounts of the antimicrobial peptide and that in this case the tumor would grow slowly and finally some EJ cell clones would not express the antimicrobial peptide at all resulting in normal growth rate of the tumor. The results shown in Figures 9 and 10 of the specification correspond well with these expectations. For some EJ clones the transfection with the cecropin gene completely prevented tumor growth (Figures 9C and 9G), other EJ clones produced tumors of a reduced size (Figures 9B, 9E and 9F) and in only one clone (Figure 9D), the transfection had no effect on the tumorigenicity. Taking the results of all animal experiments together, it is obvious that the average tumor size of mice treated with EJ cells, which were transfected with a retroviral vector comprising cecropin, compared to mice treated with normal EJ cells was significantly reduced. Clearly, the antimicrobial peptide cecropin had an antitumor effect. Similar results were obtained for melittin (see Figure 10). Consequently, the present invention provides a method of reducing (*i.e.*, treating) the size of a tumor *in vivo*. This is also true for *ex vivo* gene therapy, according to which the retroviral vector comprising the gene encoding the antimicrobial peptide is introduced into an isolated cell *in vitro*. In this case, the cells with the highest antimicrobial or antitumor activity can be selected and only those cells will be reintroduced into the organism. Hence, the present invention provides an efficient method for tumor therapy.

The Examiner further states that “[a]nother important factor needs to be considered for therapeutic use is the side effects of these AMPs and derivatives” and that “[w]hen given by a systemic method to a mammal host, the effect to normal cells of the host has to be evaluated” (Office Action, page 8).

Applicants respectfully disagree that this is a requirement for patentability. The court has clearly stated that:

[t]here is nothing in the patent statute... which gives the Patent Office the right or duty to require an applicant to prove that compounds or other materials which he is claiming, and which he has stated are useful for “pharmaceutical applications”, are safe, effective and reliable for use with humans. It is not for us or the Patent Office to legislate and if the Congress desires to give this responsibility to the Patent Office, it should do so by statute (*In re Krimmel* 130 U.S.P.Q. 215, 220 (CCPA 1961)).

Generally speaking, all pharmaceutical applications have some side effects. Applicants' data show that their claimed construct was successfully delivered and that the antimicrobial peptide was expressed *in vitro* and *in vivo* in an acceptable animal model, *and* that the antimicrobial peptide produced antitumor and antiretroviral effects with a degree of safety (*i.e.*, no major harm to the animal model was indicated). Clearly, Applicants have met their burden under 35 U.S.C. 112, first paragraph.

Furthermore, the gene encoding the antimicrobial peptide may be expressed under the control of a tissue-specific promoter, and thus, the toxic peptide may be targeted to specific predetermined cells (specification, page 14, line 19 to page 16, line 14). In this case, the antimicrobial peptide is only produced in the specific target cells, whereas all other cells are not affected by the toxic effects of the antimicrobial peptides. For example, if the promoter is tumor cell-specific, the antimicrobial peptides are only expressed in tumor cells. Using an HIV promoter, the antimicrobial peptides will be expressed only in HIV infected cells (specification page 15, line 25 to page 16, line 2). Hence the method according to the present invention allows the specific treatment of target cells *in vivo* without affecting other cells.

Clearly, Applicants have provided an enabling disclosure for the full scope of the claimed invention.

Rejection of Claims 1-26 under 35 U.S.C. §112, first paragraph

Claims 1-26 are rejected under 35 U.S.C. §112, first paragraph "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention" (Office Action, page 8). The Examiner states that Claims 1, 9, 23 exclude "defensin", however, "the reason to such exclusion has not disclosed in the specification" (Office Action, page 8). The Examiner concludes that the claims "introduced new matter to the claims" (Office Action, page 8).

Applicants respectfully disagree. There is no requirement that Applicants provide a reason for the exclusion in the specification as filed. Furthermore, the addition of a proviso does not raise a *per se* presumption that new matter is added (*Ex parte Parks*, 30 U.S.P.Q. 90, 96 (C.C.P.A. 1976)). The subject matter of the claim need not be described literally (*i.e.*, word for

word) in order for the disclosure to satisfy the description requirement (*In re Wertheim*, 191 U.S.P.Q. 90,96 (C.C.P.A. 1976)). See also M.P.E.P. §2163.02. Description can be found in the teachings taken as a whole the addition of a proviso does not raise a *per se* presumption that new matter is added (*Ex parte Parks*, 30 U.S.P.Q. 90, 96 (C.C.P.A. 1976)). The subject matter of the claim need not be described literally (i.e., word for word) in order for the disclosure to satisfy the description requirement (*In re Wertheim*, 191 U.S.P.Q. 90,96 (C.C.P.A. 1976)). See also M.P.E.P. §2163.02. Description can be found in the teachings taken as a whole.

The Court of Customs and Patent Appeals has stated that:

[W]e must decide whether the invention appellants seek to protect by their claims is part of the invention that appellants have described *as theirs* in the specification. That what appellants claim as patentable to them is *less* than what they describe as their invention is not conclusive if their specification also reasonably describes that which they do claim. Inventions are constantly made which turn out not to be patentable, and applicants frequently discover during the course of prosecution that only a part of what they invented and originally claimed is patentable. . . . To rule otherwise would let form triumph over substance, substantially eliminating the right of an applicant to retreat to an otherwise patentable species merely because he erroneously thought he was first with the genus when he filed. (Emphasis in original). *In re Wertheim* at 97.

In *In re Johnson and Farnham*, 194 U.S.P.Q. 187 (C.C.P.A. 1977), the court found that Appellants' exclusion of two species from an original genus claim to avoid having the claims read on a lost interference count was supported by the specification. The application mentioned by name fifty specific precursor compounds, E, and a description of an E' precursor as well as 26 examples of 15 species of polyarylene polyethers formed from E and E'. The pertinent portion of the claims in question read:

. . . with the provisos that E and E' may not both include a divalent sulfone group and may not both include a divalent carbonyl group linking two aromatic groups. (Emphasis in original). *Id.* at 191.

The court stated that:

. . . Appellants . . . are narrowing their claims, and the full scope of the limited genus now claimed is supported in appellants' earlier application, generically and by specific examples.

The notion that one who fully discloses, and teaches those skilled in the art how to make and use, a genus and numerous species therewithin, has somehow failed to disclose, and teach those skilled in the art how to make and use, that genus minus two of those species, and has thus failed to satisfy the requirements

of § 112, first paragraph, appears to result from a hypertechnical application of legalistic prose relating to that provision of the statute. *Id.* at 196.

In the instant specification, Applicants teach that the antimicrobial peptides include “defensin peptides or derivatives thereof” (specification, page 9, line 8). Accordingly, a person skilled in the art would recognize from the specification, as originally filed, that Applicants had possession of the presently claimed retroviral vectors at the time the subject application was filed.

Thus, the specification sufficiently describes the claimed invention and Applicants have satisfied the requirements under 35 U.S.C. §112.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (781) 861-6240.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By Anne J. Collins
Anne J. Collins

Registration No. 40,564

Telephone (781) 861-6240

Facsimile (781) 861-9540

Lexington, Massachusetts 02421-4799

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